UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/975,011	10/12/2001	Michal Amit	01/22631	8513

7590 08/21/2003

G. E. EHRLICH (1995) LTD.
c/o ANTHONY CASTORINA
SUITE 207
2001 JEFFERSON DAVIS HIGHWAY
ARLINGTON, VA 22202

EXAMINER
CROUCH, DEBORAH

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 08/21/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/975,011	AMIT ET AL.	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-24 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-24 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 12 October 2001 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Claims 1-24 are pending.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of establishing a clonal human embryonic stem cell line comprising culturing human embryonic stem cells in the presence of feeder cells, serum free medium, isolating a single stem cells, culturing the stem cell in the presence of feeder cells, serum free media and bFGF, does not reasonably provide enablement for a method of establishing a clonal embryonic stem cell line as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The culture conditions enabled by the specification for establishing human clonal embryonic stem cells are: culturing an isolated stem cell in serum free media, on feeder cells and in the presence of bFGF. It would be unpredictable to arrive at clonal human embryonic stem cells using other culture conditions. Thomson taught that the growth factors that enhanced mouse ES cell to grow and remain undifferentiated had the opposite effect on human ES cells – cellular differentiation (page 145, parag. 1, lines 10-15). Thus it is unpredictable as to the growth conditions required for human ES cell growth and remain in the undifferentiated state. Thus at the time of the instant invention, the skilled artisan would have needed to engage in an undue amount of experimentation to make the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-24 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Amit et al. (2000) Developmental Biology 227, pp. 271-278.

Amit teaches the production of human ES cell clonal cell lines where the cell lines are cultured continuously for 12 months and retained ES cell phenotypes as claimed as claimed (pages 274, 276 and 277). Amit also teaches clonal human ES cells (page 277, col. 1, parag. 1, lines 19-21). Thus Amit clearly anticipates the claimed invention.

This rejection can be overcome by filing a declaration under 37 CFR 1.132 stating that the authors on the reference, but not designated as inventors did not contribute the inventive concept.

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8 and 10-12 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Thomson et al (1998) Science 282, pp. 1145-1147.

Thomson teaches the culture of human ES cell line H9 for more than eight months (page 1145, col. 2 to col. 3, bridg. sentence). Thomson teaches the culture of many individual H9 cells. As the methods of culture in claim 1 are anticipated by Thomson, the phenotypes of the cells produced by claim 1 would be inherent properties of the cells of Thomson. Further, teaches the culture of H9 cells on mouse embryonic fibroblast feeder cells (page 1145, figure 1(A). Thus, Thomson clearly anticipates the claimed invention

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of

> paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 17-24 rejected under 35 U.S.C. 102(e) as being clearly anticipated by U.S. Patent 6,576,464 B2 (Gold).

Gold teaches clonal human embryonic stem cell lines H9.1 and H9.2 (col. 30, lines 21 and 22, Table I). H9.1 and H9.2 are disclosed in the specification as being clonal human embryonic stem cell lines that meet the limitations of the claims. All of the limitations to the cells claimed are inherent properties of H9.1 and H9.2. Therefore, Gold teaches the claimed invention.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomson et al (1998) Science 282, pp. 1145-1147 in view of WO 97/32033 published (Hogan.

Thomson teaches the culture of human ES cell line H9 for more than eight months (page 1145, col. 2 to col. 3, bridg. sentence). Thomson teaches the culture of many individual H9 cells and that the H9 cells give rise all three germ layers, a normal phenotype of ES cells (page 1146, col. 1, parag. 2, lines 1-3). However, Thomson does not teach the culture of human ES cells in the presence of bFGF. Hogan teaches the culture of embryonic stem cells in the presence of 0.5-500 ng/ml bFGF (page 32, lines 17-24 and page 33, lines 21-25). Motivation is provided by Hogan in stating that bFGF is proliferation enhancing and directs the use of the method to human ES cells (page 33, lines 21-22 and page 34, lines 15-16). Thus, it would have been obvious to the ordinary artisan to develop a method of establishing clonal stem cell line in culture using the method of Thomson and including bFGF as taught by Hogan. The cited prior art provides the requisite teaching, suggestion and motivation for the ordinary artisan at the time of filing to make the claimed invention.

Claims 1, 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomson et al (1998) Science 282, pp. 1145-1147 in view of Thomson et al (1995) Proceed. Natl. Acad. Sci. 82, pp. 7844-7848.

Thomson teaches the culture of human ES cell line H9 for more than eight months (page 1145, col. 2 to col. 3, bridg. sentence) and that they maintain a normal ES cell phenotype of cell surface antigens (page 1145, col. 3, 2, 1-7). However, Thompson (1998) does not teach clones of H9 (). Thomson (1995) teaches the clonal culture of rhesus monkey clonal embryonic stems cells on a mouse embryonic fibroblast feeder culture (7845, 1, 4-8). The cells of Thomson (1995) maintain the ability to develop into all three germ layers (page 7846, col. 2, lines 5-6). Motivation is offered by Thomson (1998) in suggesting that cloned human ES cells would lack a variation in developmental potential (page 1146, col.1 , parag. 1, lines 15-20). Thus at the time of the instant invention, it would have been obvious to the ordinary artisan to clone human ES cells grown for eight

months as taught by Thomson (1998) using the methods for cloning rhesus monkey ES cells taught by Thomson (1995) so that a cell line would be produced where the developmental potential would be identical through out the population. The cited prior art provides the requisite teachings, suggestions and motivation at the time of filing for the ordinary artisan to have a reasonable expectation of success at reaching the claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 703-308-1126. The examiner can normally be reached on M-Th, 8:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Deborah Crouch

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

dc
August 9, 2003